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(54) Title: DIFFERENTIALLY EXPRESSED GENES INVOLVED IN ANGIOGENESIS, THE POLYPEPTIDES ENCODED THEREBY, AND METHODS OF USING THE SAME

(57) Abstract: The present invention is directed to nucleic acid sequences and the polypeptides encoded thereby that are differentially expressed in angiogenesis. Also provided are methods for stimulating or inhibiting angiogenesis in mammals, including humans. Pharmaceutical compositions based on polypeptides, agonists, or antagonists thereto are also provided. Additionally, the invention also provides methods for diagnosing and treating angiogenic disorders including, but not limited to, wound healing and cancer.

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最終頁に続く

(54)【発明の名称】 脈管形成に含まれる差動発現遺伝子、それにコードされるポリペプチド、及びそれを用いた方法

(57)【要約】

本発明は、核酸配列及びそれによりコードされるポリペプチドに係り、それらは脈管形成において差動的に発現される。また、ヒトを含む哺乳動物において脈管形成を刺激又は阻害する方法も提供される。ポリペプチド、それに対するアゴニスト又はアンタゴニストもまた提供される。さらに、本発明は、それらに限定されないが創傷治癒及び癌を含む脈管形成障害の診断及び治療のための方法も提供する。

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This image shows a full page of dot grid paper. It consists of multiple horizontal rows of small, evenly spaced black dots on a white background. The dots are arranged in straight lines across the entire width of the page, providing a guide for writing or drawing without solid lines.

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This image shows a single sheet of white paper with ten horizontal rows of small black dots. Each row consists of approximately 60 evenly spaced dots, creating a guide for handwriting practice. The rows are parallel and extend across the width of the page.

This image shows a single sheet of white paper designed for handwriting practice. It features ten horizontal rows of small black dots, evenly spaced across the page. The first row has a shorter starting segment compared to the others. Each row contains approximately 60 dots, providing a guide for letter height and placement.

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This image shows a full page of dot grid paper. It features approximately 20 horizontal rows of small, evenly spaced black dots. The dots are arranged in straight lines across the width of the page, providing a guide for writing or drawing without solid horizontal lines. The background is white, and there are no margins or other markings present.

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This image shows a full page of primary-ruled notebook paper. It features multiple horizontal rows, each consisting of two dotted lines with a dashed midline between them. The rows are evenly spaced across the entire page, providing a guide for letter height and placement. There are no margins, text, or other markings present.

[The page contains faint dotted lines forming horizontal bands across the entire area.]

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This image shows a full page of primary-ruled paper. It contains ten horizontal rows of small, evenly spaced dots, designed for young students to practice handwriting or basic arithmetic. The rows are distributed evenly across the page, leaving margins at the top and bottom.

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This image shows a full page of dot grid paper. It features approximately 28 horizontal rows of small, evenly spaced black dots. The dots are arranged in straight lines across the width of the page, providing a guide for writing or drawing without solid horizontal lines. There are no margins, text, or other markings on the page.

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A series of horizontal dotted lines for writing.

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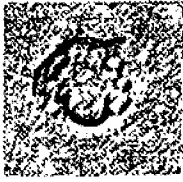


Fig. 1A

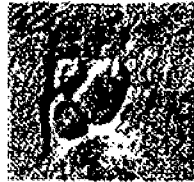


Fig. 1B

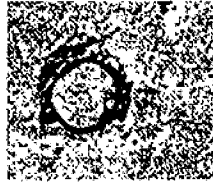


Fig. 1C

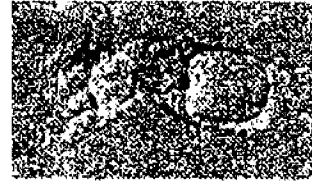


Fig. 1D



Fig. 1E



Fig. 1F



Fig. 1G

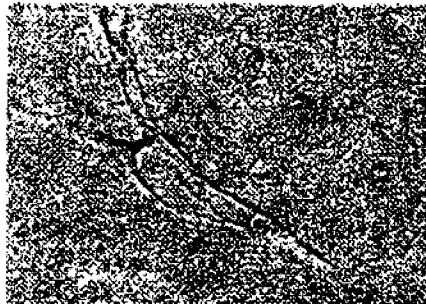


Fig. 1H



Fig. 1I

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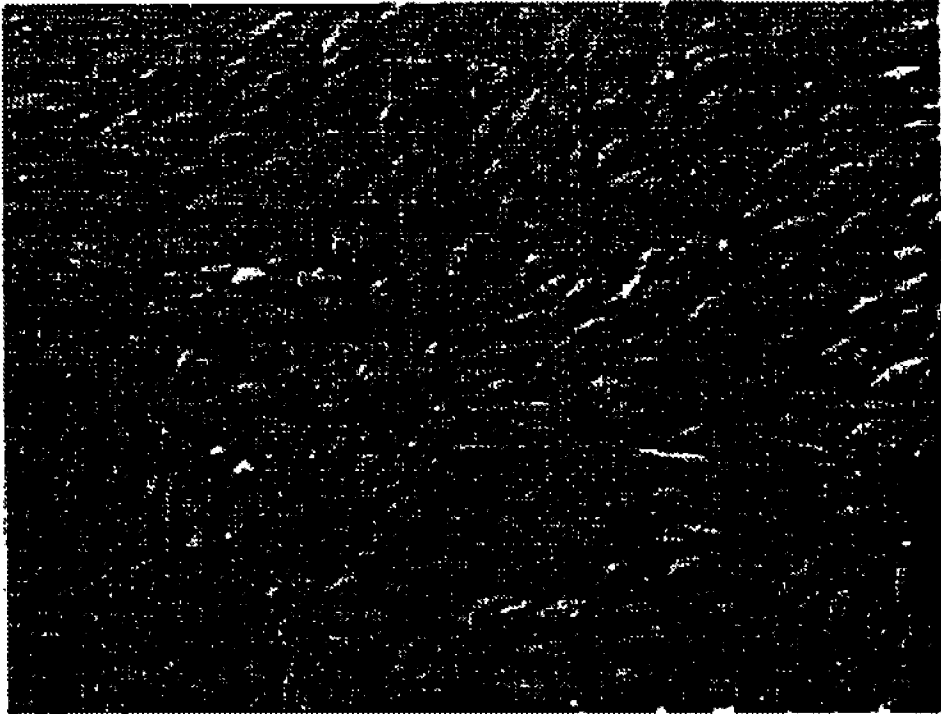


Fig. 1J

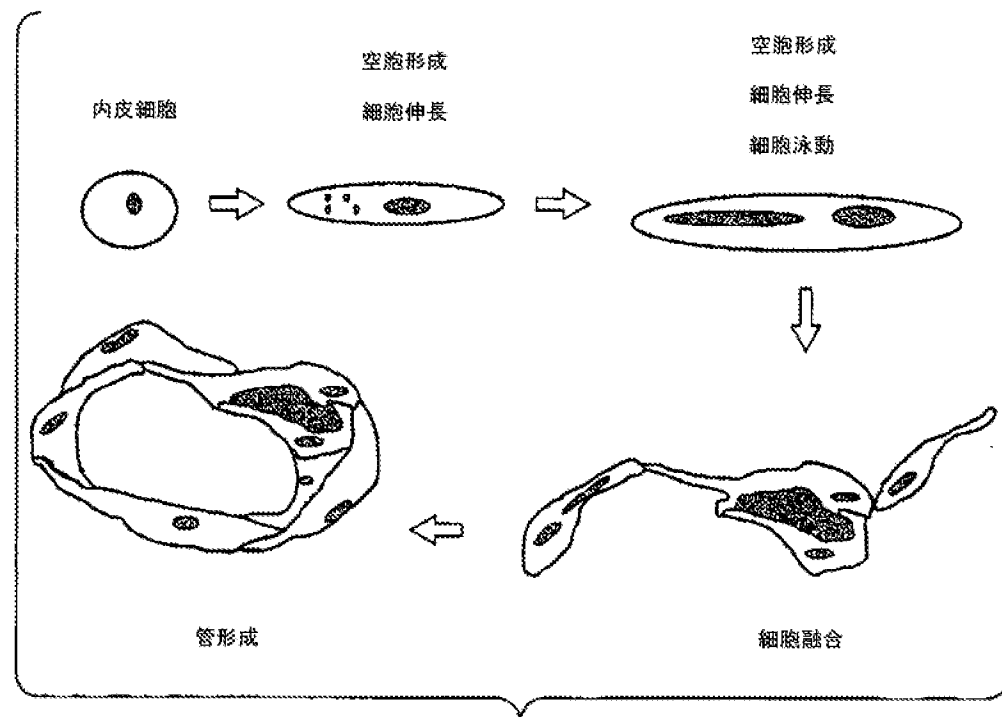


Fig. 2

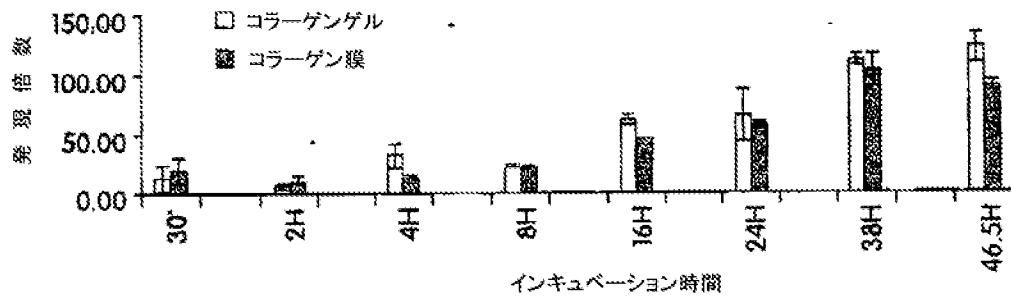


Fig. 3

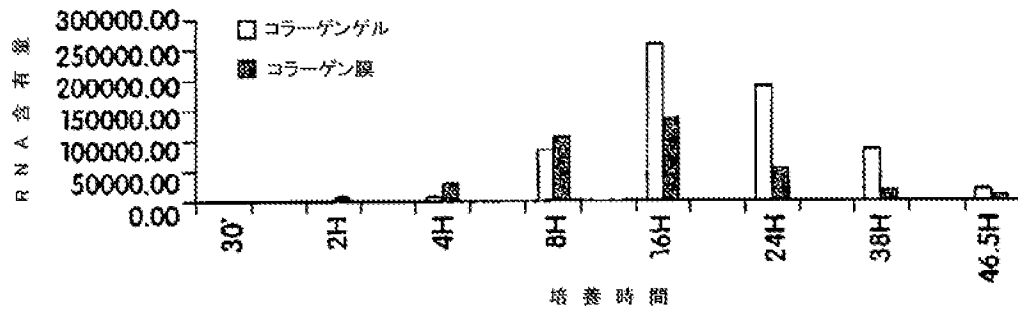


Fig. 4

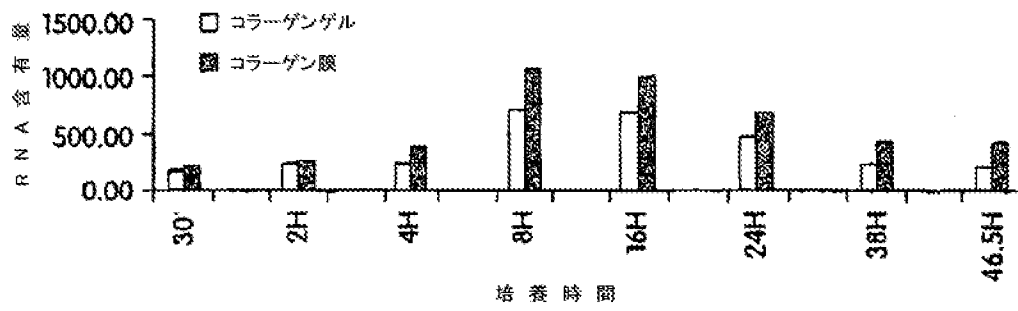


Fig. 5

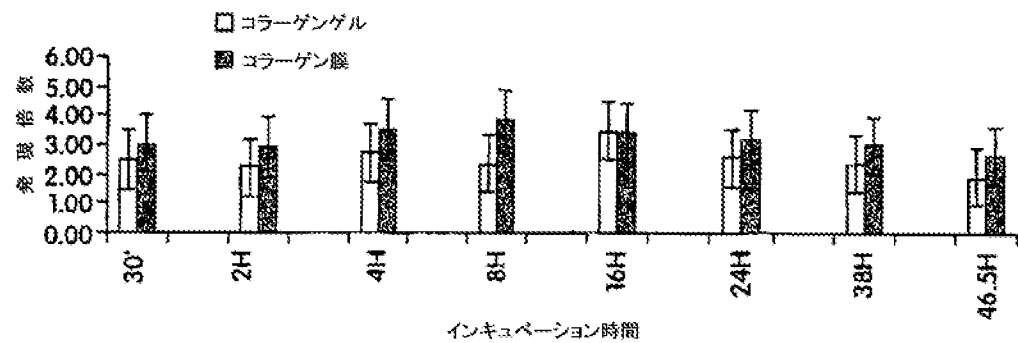


Fig. 6

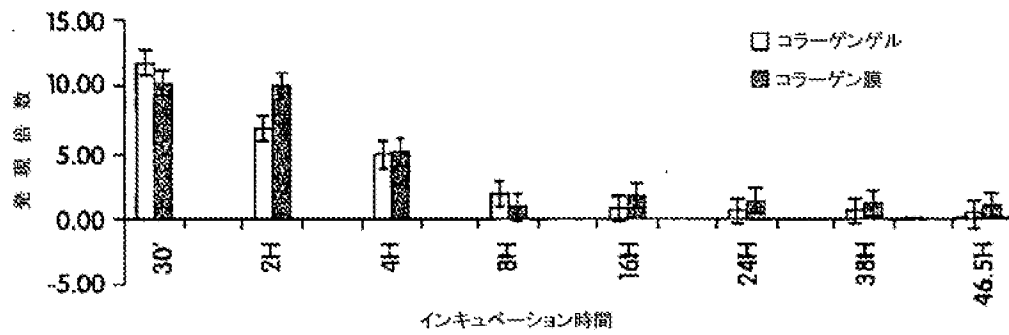


Fig. 7

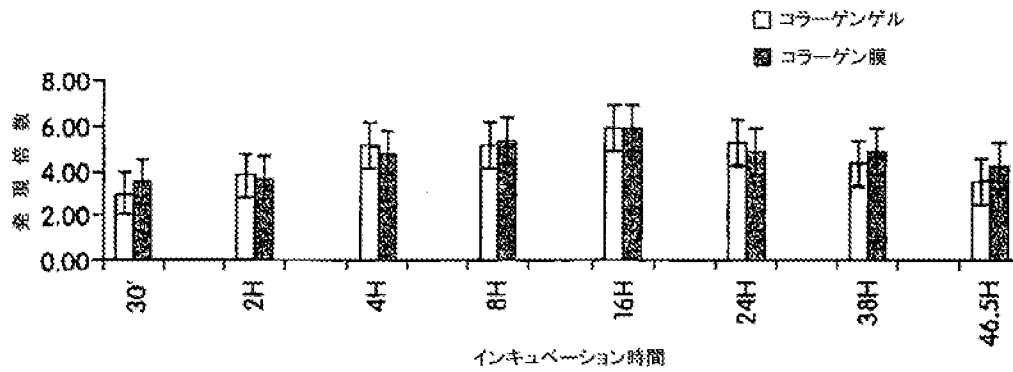


Fig. 8

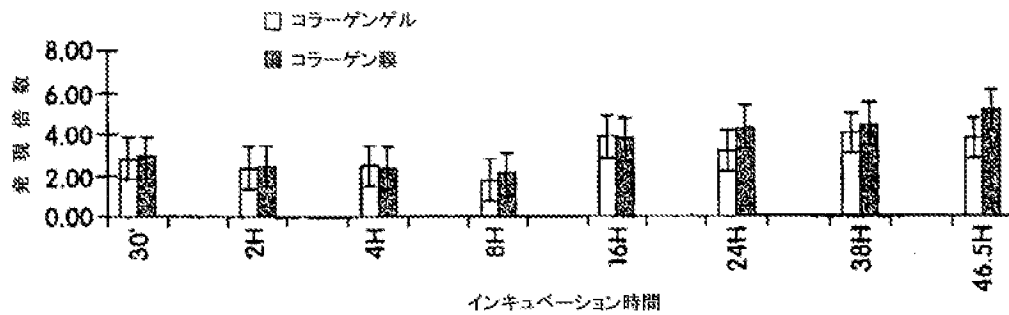


Fig. 9

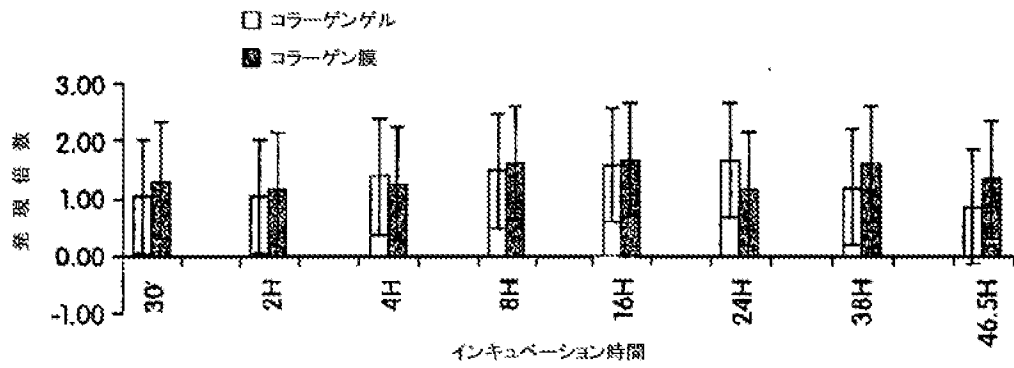


Fig. 10

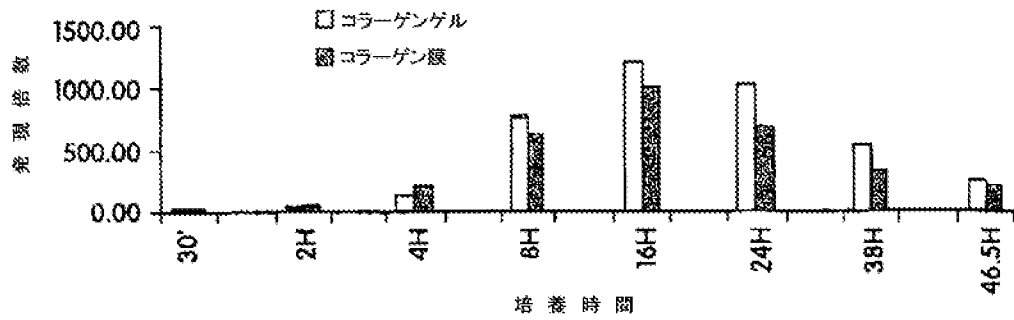


Fig. 11

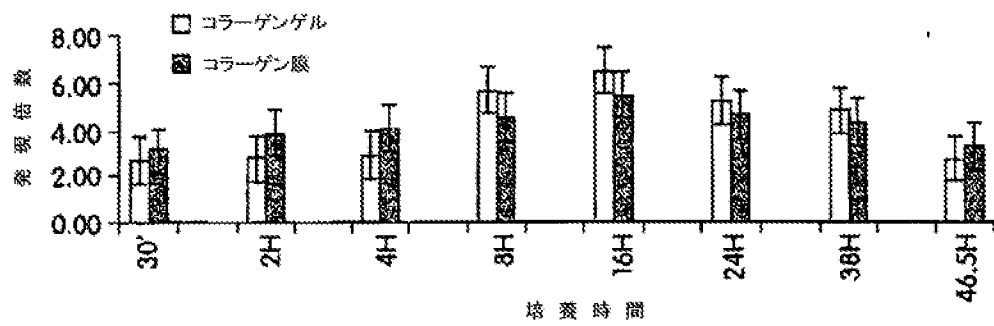


Fig. 12

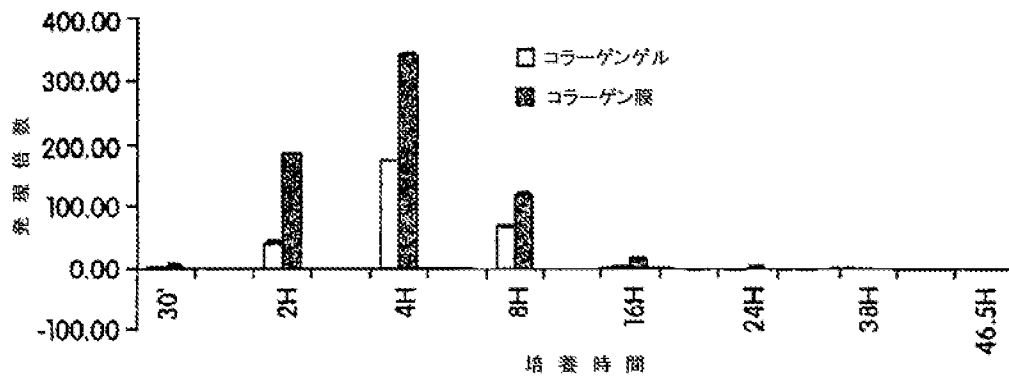


Fig. 13

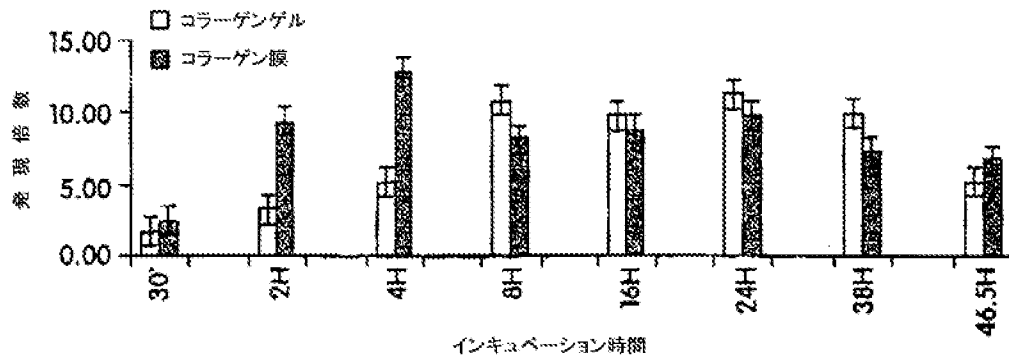


Fig. 14

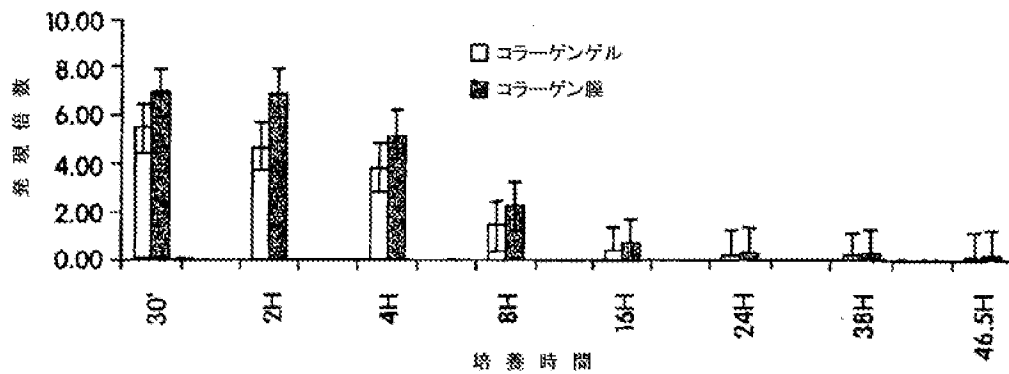


Fig. 15

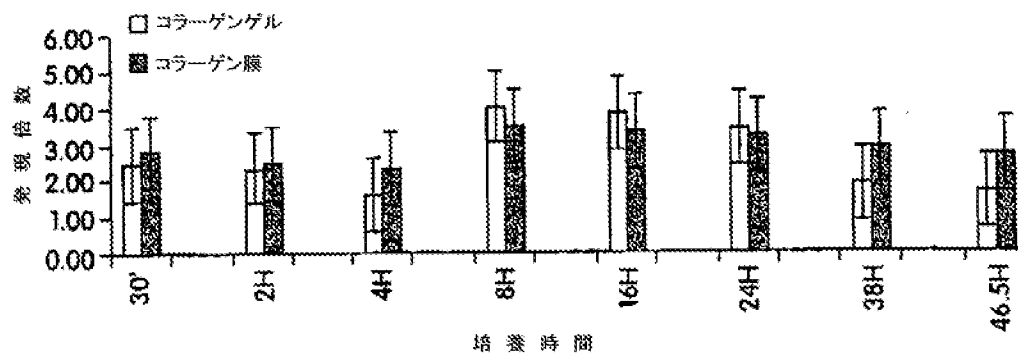


Fig. 16

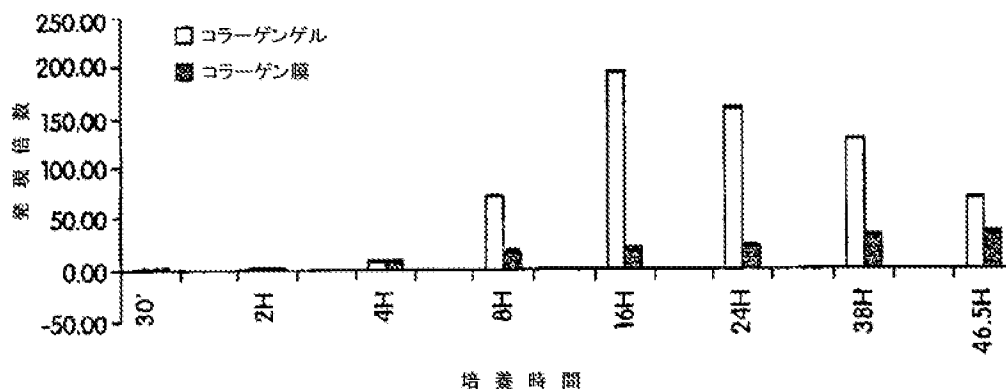


Fig. 17

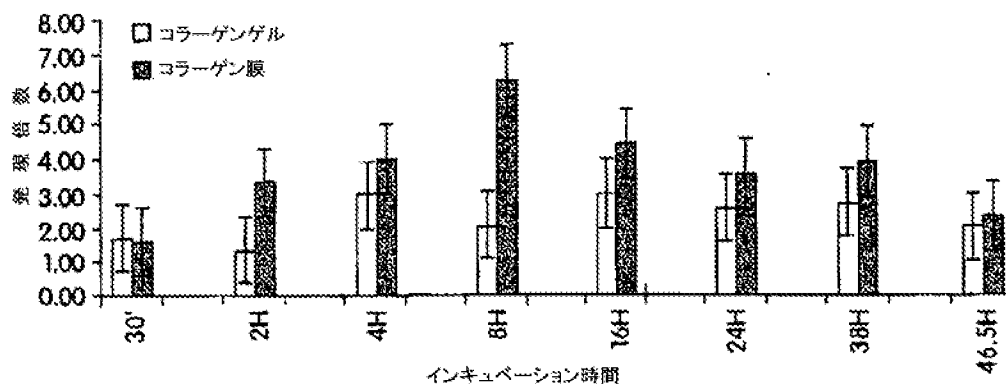


Fig. 18

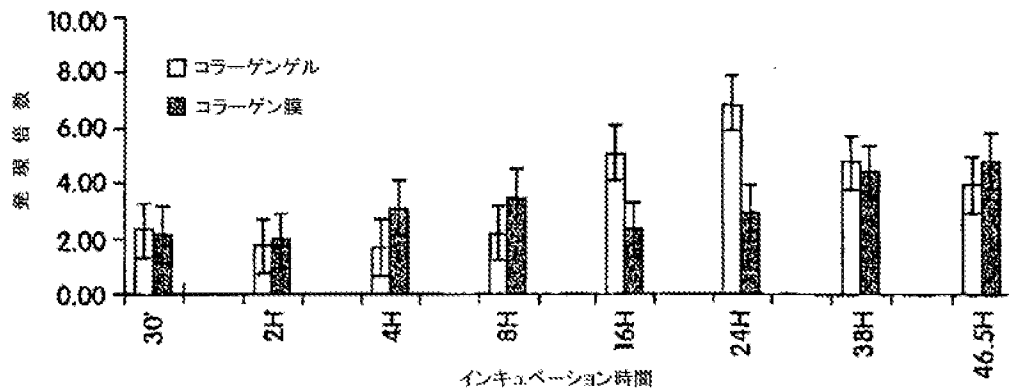


Fig. 19

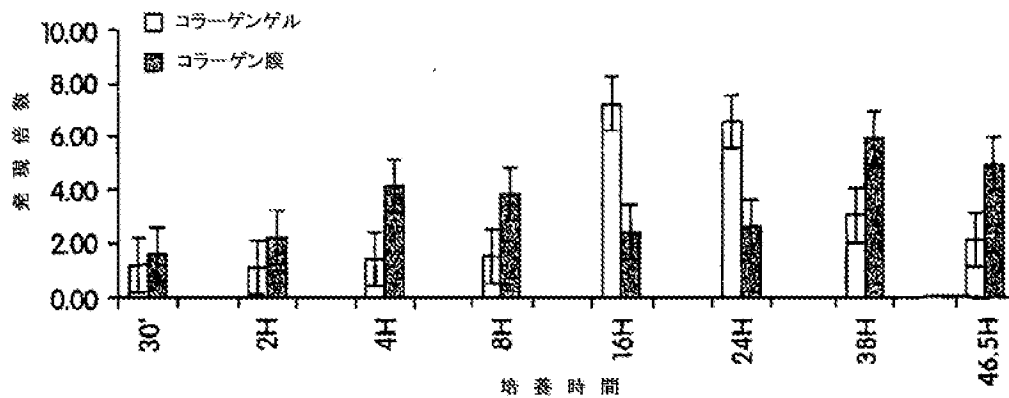


Fig. 20

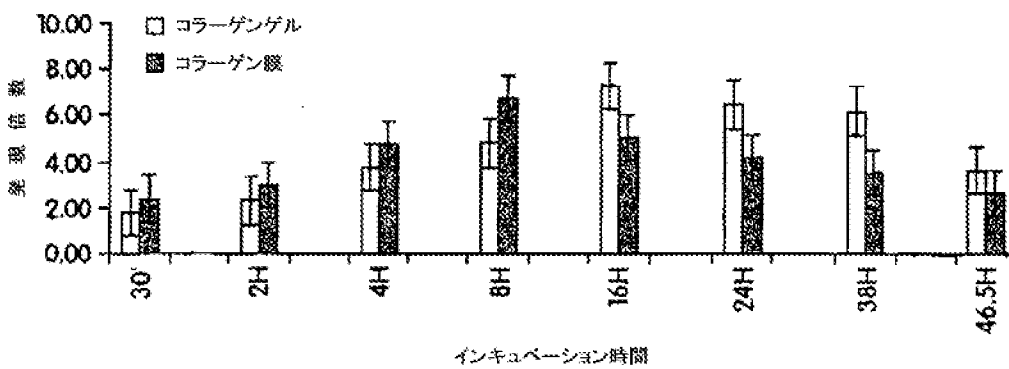


Fig. 21

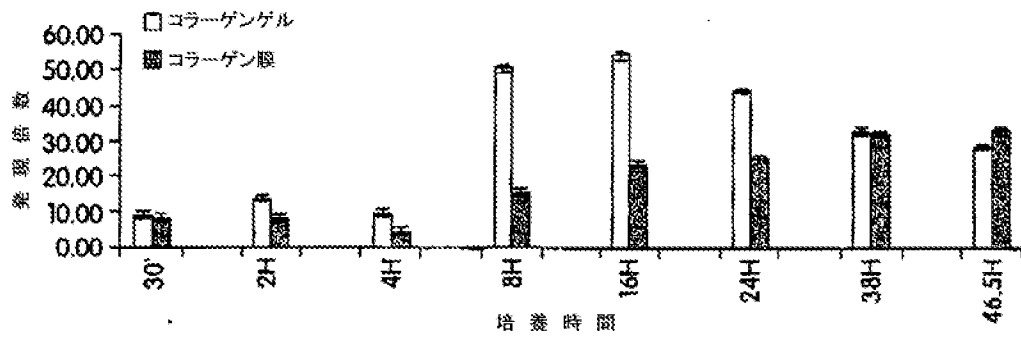


Fig. 22

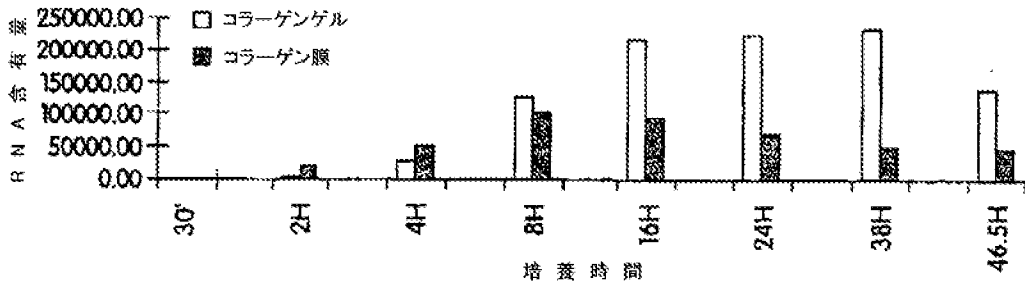


Fig. 23

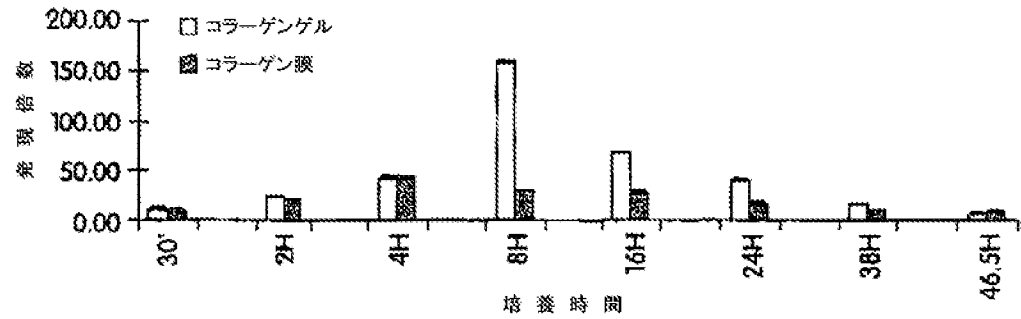


Fig. 24

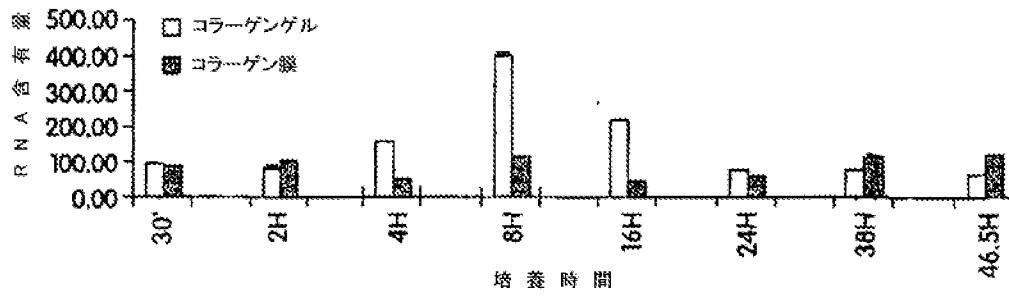


Fig. 25

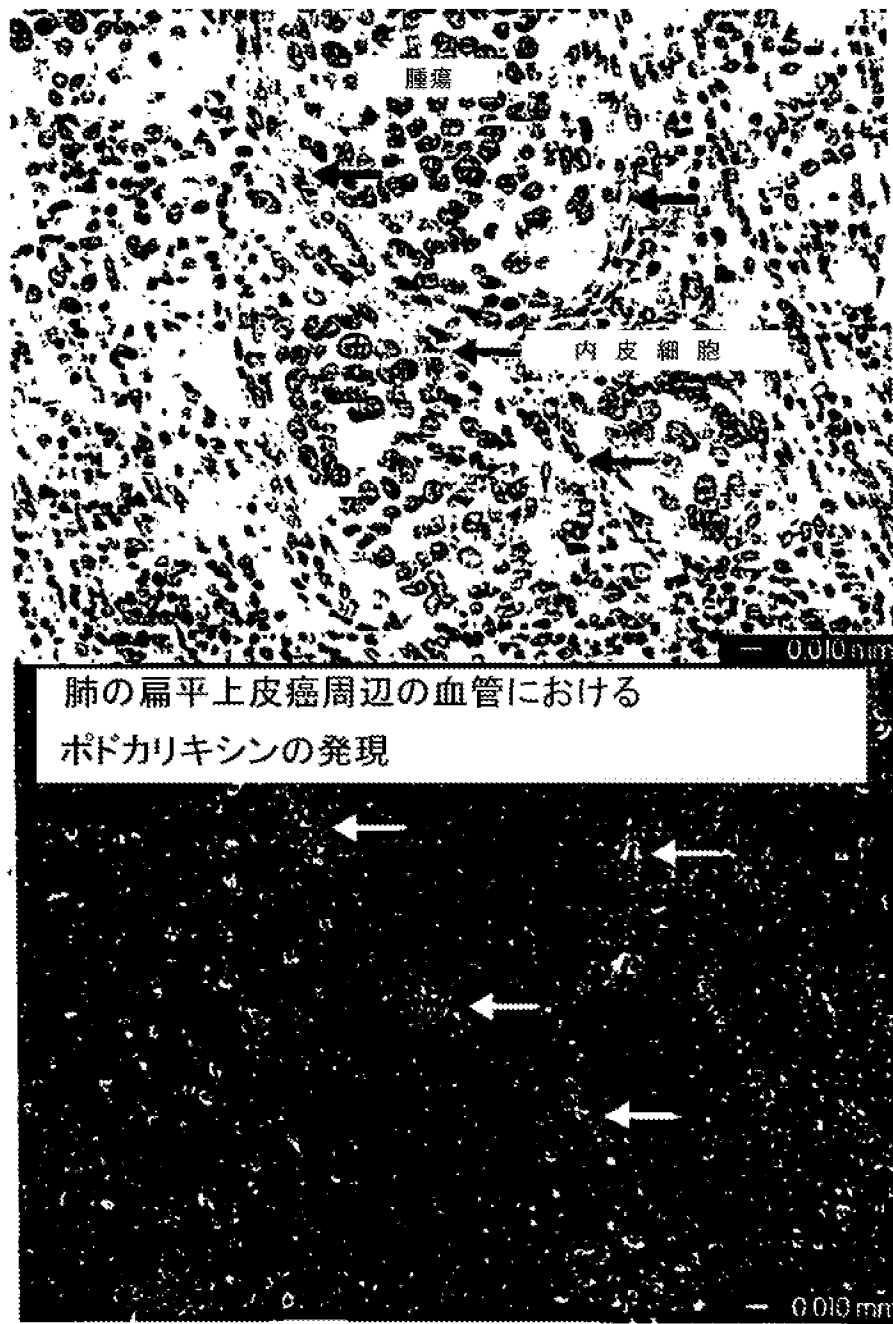


Fig. 26

肺腺癌におけるDNA76510
(プロテインゼロ相同体)の発見

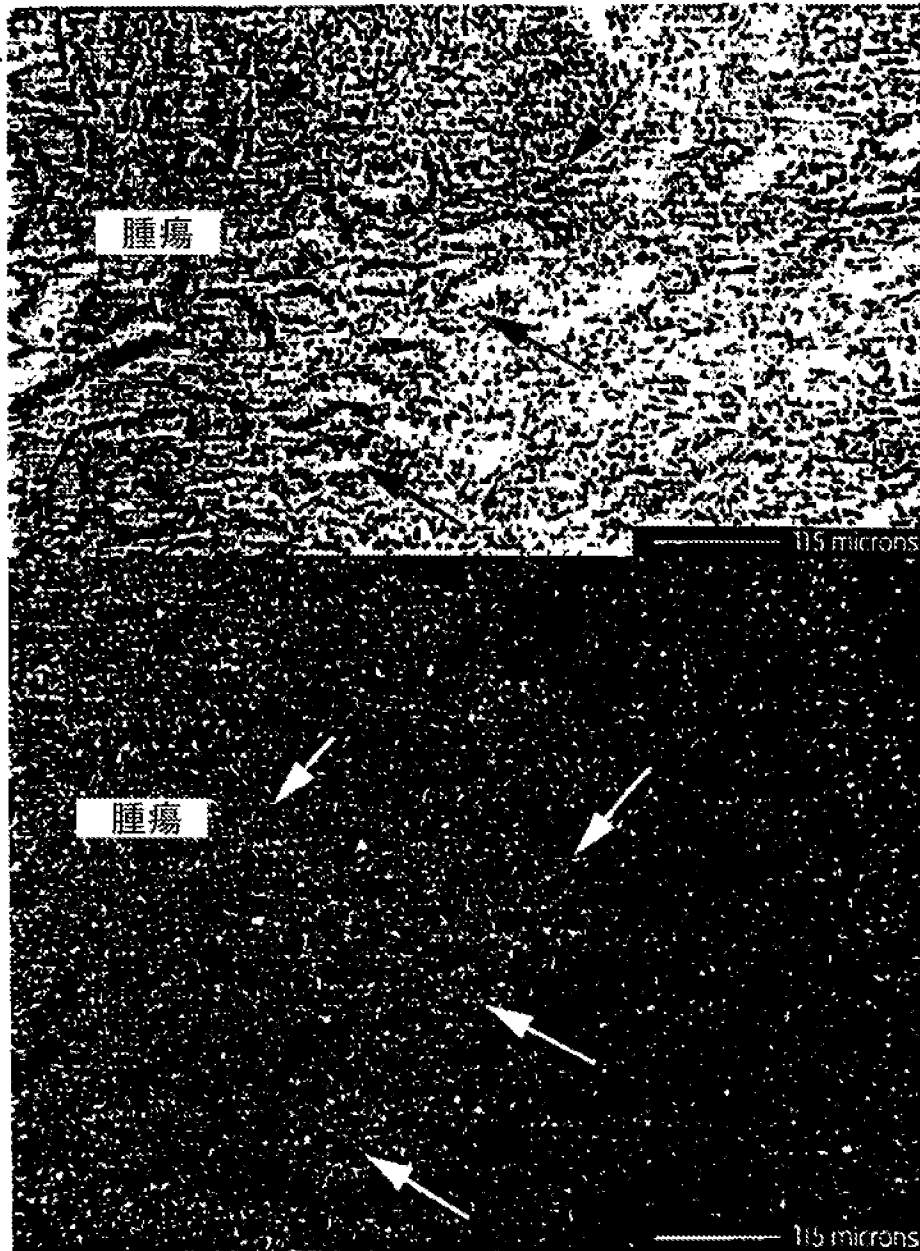


Fig. 27

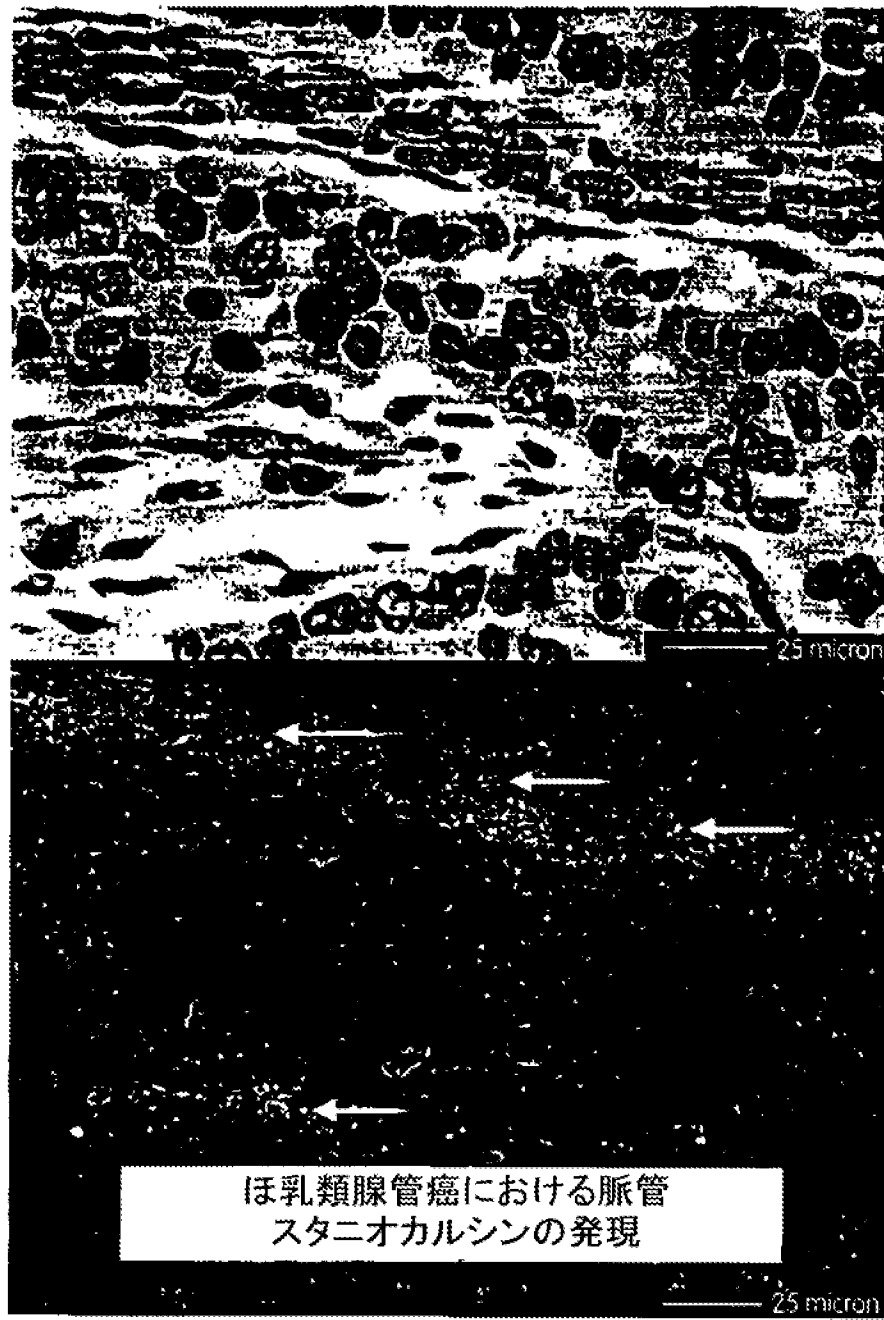


Fig. 28

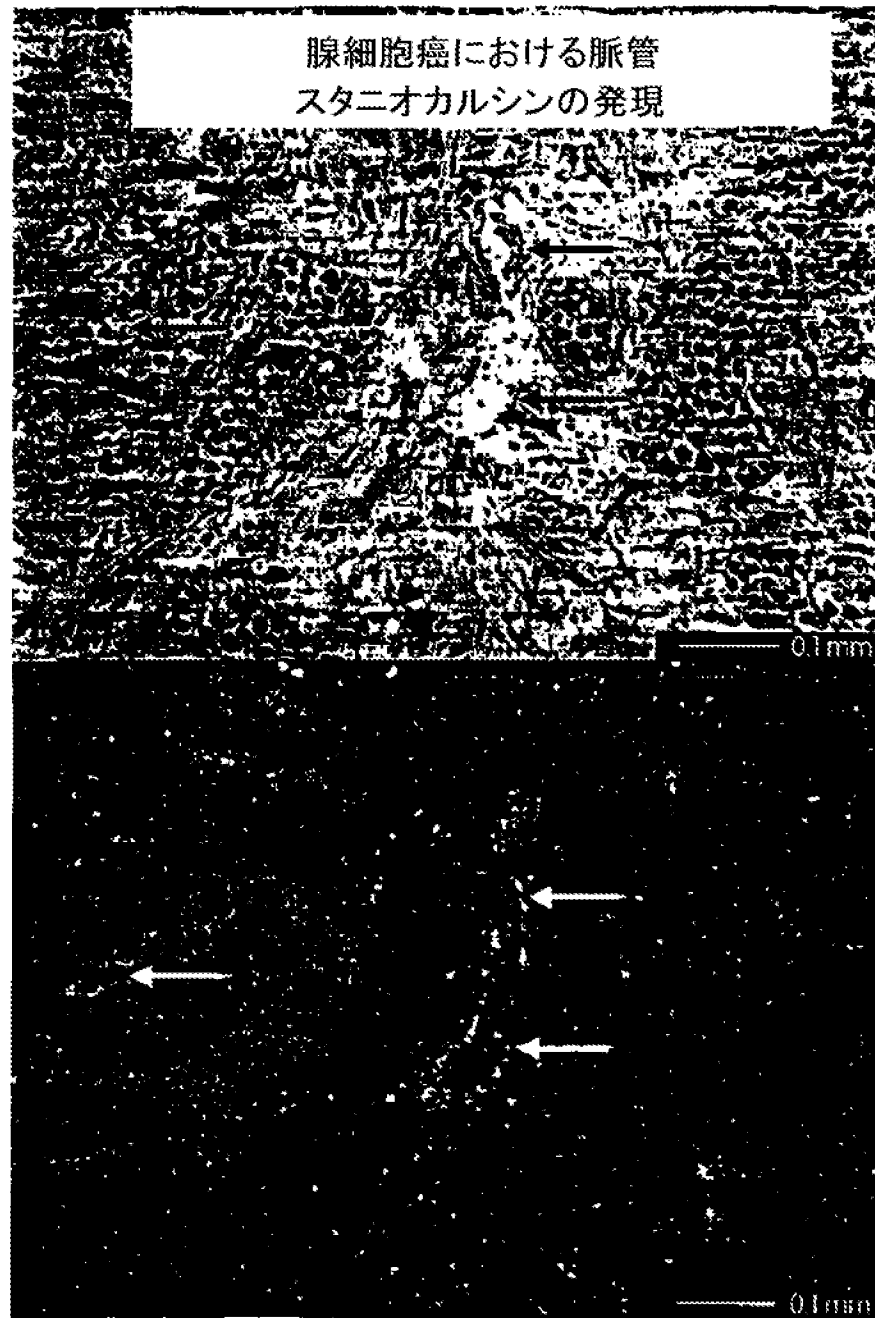


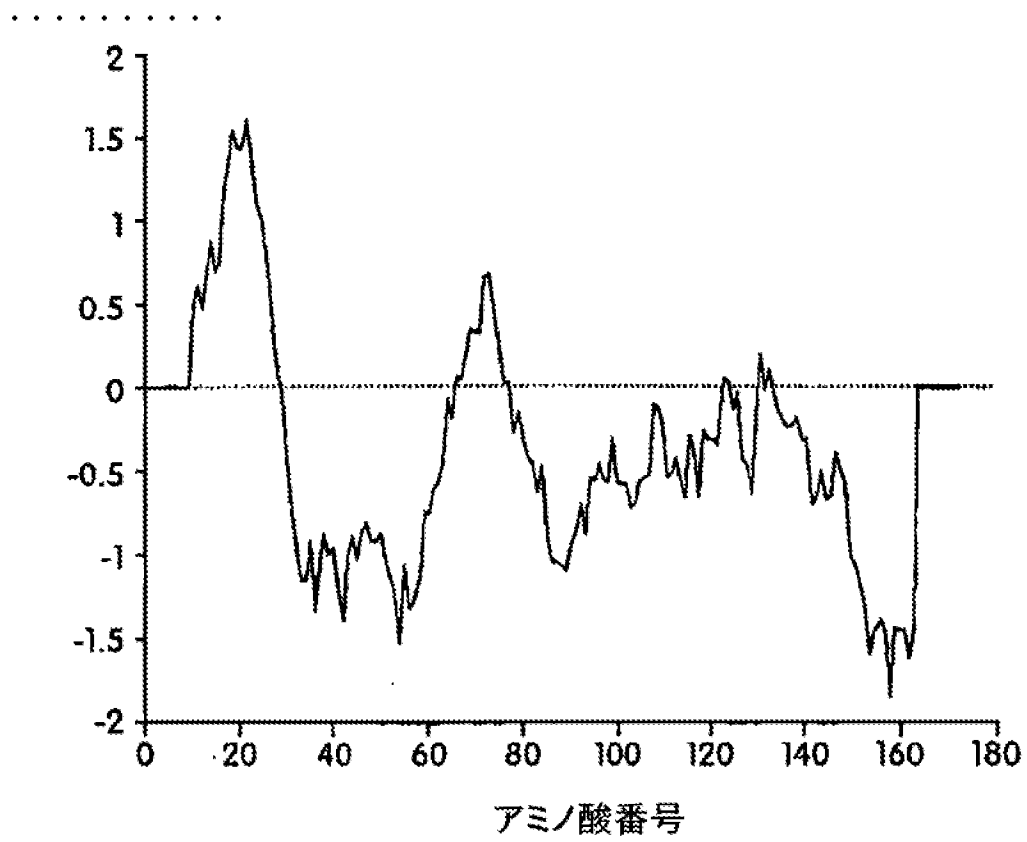
Fig. 29

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1 MVGPAPRRRLRPLAALVLALAPGLPTARAGQTFRPAERGHFVRLFTTEELARYGGEEDQPIYLAVKGVVFDVTSQKE
81 FYGRGAPYNALTGKDSTRGVAKMSLDPADLTHDTTGLTAKELLEALDEVFTKVYKAKYPIVGYTARRILNEDGSPNLDFKP
161 EDQPHFDIKDEF (配列番号: 72)

Fig. 30

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**Fig. 31**

```

Sequence type explicitly set to Protein
Sequence format is Pearson
Sequence 1: 55193557_EXT      153 aa
Sequence 2: 11725372_EXT     161 aa
Sequence 3: AF173937         172 aa
Start of Pairwise alignments
Aligning...
Sequences (1:2) Aligned. Score: 83
Sequences (1:3) Aligned. Score: 83
Sequences (2:3) Aligned. Score: 90
Start of Multiple Alignment
There are 2 groups
Aligning...
Group 1: Sequences: 2      Score:1860
Group 2: Sequences: 3      Score:1948
Alignment Score 2458
CLUSTAL-Alignment file created [/data4/genetools/iraastelli5501clustalw]

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Multiple Alignment:

```

55193557_EXT -----GAGCGPSA-ESLGNDAAR--R--
11725372_EXT -----VR-VSS-GEQ-
AF173937      MVGPAPRRRL-----VLAAPGSI-----

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Fig. 32

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This image shows a full page of primary-ruled paper. It features ten horizontal rows of small black dots, each row serving as a guide for handwriting practice. The dots are evenly spaced both horizontally and vertically across the entire page.

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表1. 差動発現データ

遺伝子名	GenBank登録番号	GeneCalling モジュレーション	TaqMan モジュレーション
オステオニドゲン (PA1)	D86425	+4	+2
ラミニン ガンマ-2 鎖 (PA2)	U31201	+18	+49
ポドカリキシン様タンパク質 (PA3)	U97519	+12	+2
モエシン (PA4)	M69066	+2	1
中皮ケラチンK 7 (II型) (PA5)	X03212	-5	-10
ミオシン-I C (PA6)	U14391	+2	ND
T-プラスチン (PA7)	L05481	+2	1
アクチン細胞タンパク質 (PA8)	U09873	+2	+2
グイニン軽鎖 (PA9)	U32944	+3	ND
C3VS相同体 (PA10)	Q28282に類似	+2	1
カテプシンB (PA11)	M14221	+3	+2
アダレカナーゼ, ADAMTS-4 (PA12)	NM_005099	+18	+2
組織因子経路インヒビター-2 (PA13)	L27624	+9	+7
ウロキナーゼ インヒビター (PA1-2) (PA14)	M31551	-19	-92
チロシンキナーゼ, レセプター-axl, alt. スプライス 2 (PA15)	P30530	-6	-15
チロシンキナーゼ, レセプター, 上皮 細胞, ECK (PA16)	NM_004431	+3	+3
OX40 (PA17)	S76792	+18	+18
インターロイキン6シグナルトランスドューサー, gp130 (PA18)	M57230	+3	1
cd82 (PA19)	D28137	+12	+4
プロテインゼロ関連タンパク質 (PA20)	AF087020	+6	+6
アルファ-2 インテグリン (PA21)	X17033	+13	+2
胎盤成長因子 (PIGF) (PA22)	X54936	+6	+5
スタニオカルシン前駆体 (PA23)	U25997	+14	+8
繊維芽細胞成長因子 (FGF-16) (PA24)	AB009391	+4	1
ホワイトプロテイン相同体 (PA25)	X91249	+3	-2
シマウスAlix (ALG-2相互作用 タンパク質) (PA26)	AJ005073に類似	+5	+2

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This image shows a full page of dot grid paper. It features approximately 20 horizontal rows of small black dots. Each row contains about 60 dots, evenly spaced across the width of the page. The dots are arranged in straight horizontal lines, providing a guide for writing or drawing without the prominence of solid lines. The background is white, and the overall layout is clean and minimalist.

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表 2

遺伝子名	薬剤標的	抗体標的	治療的蛋白質	遺伝子治療	iseaseMarke
オステオニドゲン(PA1)	XX	XX		XX	XX
タミニン ガンマ-2 鎖(PA2)	XX	XX		XX	XX
ボドカリキニン様タンパク質(PA3)	XX	XX		XX	XX
ホエニン (PA4)	XX	XX		XX	XX
中皮ケラチン K 7 (H型) (PA5)	XX	XX		XX	XX
ミオニン-1 C (PA6)	XX	XX		XX	XX
グーグラスチン(PA7)	XX	XX		XX	XX
アフラチン様タンパク質 (PA8)	XX	XX		XX	XX
グアイニン様タンパク質 (PA9)	XX	XX		XX	XX
C 3a V S 相同体(PA10)	XX	XX		XX	XX
カテプシン B (PA11)	XX	XX		XX	XX
アグレカナーゼ, ADAMTS-1 (PA12)	XX	XX		XX	XX
神経因子経路インモビター-2 (PA13)	XX	XX		XX	XX
クロキナーゼ [*] イニキター (PA1-2) (PA14)	XX	XX	XX	XX	XX
ナロンキナーゼ [*] , レセプター-nx1, alt, スプライズ 2 (PA15)	XX	XX	XX [*]	XX	XX
ナロンキナーゼ [*] , レセプター [*] クー, 上皮細胞, EEC (PA16)	XX	XX	XX [*]	XX	XX
OX40 (PA17)	XX	XX	XX [*]	XX	XX
インターフェロンβ [*] ナルトランスフェーザ, gp130 (PA18)	XX	XX	XX [*]	XX	XX
cd82 (PA19)	XX	XX	XX [*]	XX	XX
プロテインゼロ [*] 関連タンパク質(PA20)	XX	XX	XX [*]	XX	XX
アルファ-2 インテグリン (PA21)	XX	XX	XX [*]	XX	XX
新癌成長因子 (F16P) (PA22)	XX	XX	XX	XX	XX
スクニオカルシン前駆体 (PA23)	XX	XX	XX	XX	XX
遠隔芽細胞成長因子 (FOP-16) (PA24)	XX	XX	XX	XX	XX
ホワイトプロテイン相同体 [*] (PA25)	XX	XX		XX	XX
s1aマウスAlix (A1C-2相互作用タンパク質) (PA26)	XX	XX		XX	XX

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This image shows a full page of dot grid paper. It features approximately 20 horizontal rows of small black dots, evenly spaced across the page. The dots are arranged in straight lines, providing a guide for writing or drawing without solid lines. The background is white, and the overall appearance is clean and minimalist.

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<u>元の残基</u>	<u>例示的置換</u>	<u>好ましい置換</u>
Ala (A)	val; leu; ile	val
Arg (R)	lys; gln; asn	lys
Asn (N)	gln; his; lys; arg	gln
Asp (D)	glu	glu
Cys (C)	ser	ser
Gln (Q)	asn	asn
Glu (E)	asp	asp
Gly (G)	pro; ala	ala
His (H)	asn; gln; lys; arg	arg
Ile (I)	leu; val; met; ala; phe; norleucine	leu
Leu (L)	norleucine; ile; val; met; ala; phe	ile
Lys (K)	arg; gln; asn	arg
Met (M)	leu; phe; ile	leu
Phe (F)	leu; val; ile; ala; tyr	leu
Pro (P)	ala	ala
Ser (S)	thr	thr
Thr (T)	ser	ser
Trp (W)	tyr; phe	tyr
Tyr (Y)	trp; phe; thr; ser	phe
Val (V)	ile; leu; met; phe; ala; norleucine	leu

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A grid of 10 rows of dotted lines for handwriting practice. The first row has 20 dots, the second has 20 dots, the third has 20 dots, the fourth has 20 dots, the fifth has 20 dots, the sixth has 20 dots, the seventh has 20 dots, the eighth has 20 dots, the ninth has 20 dots, and the tenth has 20 dots.

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This image shows a full page of dot grid paper. It features approximately 20 horizontal rows of small, evenly spaced black dots. The dots are arranged in straight lines across the width of the page, providing a guide for writing or drawing without solid lines. The background is white, and the overall appearance is clean and minimalist.

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This image shows a full page of dot grid paper. It features approximately 20 horizontal rows of small, evenly spaced black dots. The dots are arranged in straight lines across the width of the page, providing a guide for writing or drawing without solid horizontal lines. There are no vertical margin lines or other markings present.

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[The page contains faint dotted horizontal lines for writing.]

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This image shows a full page of dot grid paper. It features approximately 20 horizontal rows of small black dots. Each row contains about 60 dots, evenly spaced across the width of the page. The dots are arranged in straight, parallel lines, creating a guide for writing or drawing. There are no margins, text, or other markings on the page.

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表 4. Taqmanプライマー及びプローブの組

遺伝子名	PA #	正方向プライマー	逆方向プライマー	プローブ
ホルモン/成長因子				
胎盤成長因子 (PlGF)	22	GACGTTCTTCAGCAGCTTCG (SEQ ID NO:3)	CACCTTTCGGGCTTCATCTTC (SEQ ID NO:4)	CCGAATGCCGGCCTCTGCGG(SEQ ID NO:5)
スタニオニカルシン前駆体 ID NO:6)	23	CGAGTGGCGGCTCAAAA(SEQ ID NO:6)	CCGCAGCCGACCTGTAGA (SEQ ID NO:7)	TCAGCTGAAGTGGTTGCTTGCCTCAA(SEQ ID NO:8)
繊維芽細胞成長因子 (SEQ ID NO:9)	24	CCTTAGCTGACTCCCCAGGTT (SEQ ID NO:9)	CTGCAGCTTCCCTCCGATT (SEQ ID NO:10)	CCTGAACGAGCCCTGGGCC(SEQ ID NO:11)
16 (FGF-16)				
チロシンキナーゼレセプター...				
ax1	15	GCATGAAGGAATTTGACCAT (SEQ ID NO:12)	TCTCTGTTTCAGAACGCTGGA (SEQ ID NO:13)	CAGACACCGATGAGCCTCATGACCTT(SEQ ID NO:14)
上皮細胞チロシンキナーゼ (Eck)	16	GCCTGTTCAACCAGATTGACA (SEQ ID NO:15)	GCCTCGAAGTCCCTGCTGSE Q ID NO:16)	TTGGCCCGATGAGATCACCG(SEQ ID NO:17)
他のレセプター... / ...体膜糖タンパク質				
OX40	17	CCAACTCTGCACCGTTCTTAGG (SEQ ID NO:18)	GGTATGCAATGACATACGTAA GC(SEQ ID NO:19)	CCGATGGCTGGCTTCGGGCT(SEQ ID NO:20)
ボトカリキシン様タンパク質	3	GGGCATGGTGAGGTTTCATCT (SEQ ID NO:21)	TTTACGCCCCAGAACGATGG (SEQ ID NO:22)	CCATGGCGAAAGTTCAACATTTCCACA(SEQ ID NO:23)
アルファ-2 インテグリン	21	TCTGAGACTGCCAAGGTTCTTC (SEQ ID NO:24)	CAGCTGGTATTTTTCGGACAT C(SEQ ID NO:25)	AGGACTAGATCAAGAAATGCCAAAGTCCATCCTCA (SEQ ID NO:26)
Gp130	18	ATCCGGCCAGAGATGTTGAC (SEQ ID NO:27)	ACCTGTAGATTCAGTGGTGAG GAAA(SEQ ID NO:28)	ACAAGGCTTGCACCTACCCAAAGTCTGCA(SEQ ID NO:29)
プロテインゼロ関連 タンパク質	20	TGTGTCATATCAATTTCTGGA (SEQ ID NO:30)	TTGATCCAACTGTGTCCAGAA TTCATA(SEQ ID NO:31)	TGACTTGGGCATTTATCCTTTTCTTAACTTGTCT(S EQ ID NO:32)
CD82	19	CGACACGTGGGCACAGG(SEQ ID NO:33)	AGCTTCTTCCACGAAACCA (SEQ ID NO:34)	CAGCTGGTGCACAGGCGCCACTTCT(SEQ ID NO:35)

プロテアアーゼ/プロテアーゼインヒビター...

組織因子経路インヒビター-2 (TFPI-2)	13	CGATGCTGCTGGAGGATAG A (SEQ ID NO:36)	AACTGTCGTCACACTCAC T (SEQ ID NO:37)	AAAGTCCCAAAGTTTCCCGGCTGC (SEQ ID NO:38)
アダマシム-2 (ADAMTS4)	12	ACTGGTGGTGGCAGATGACA (SEQ ID NO:39)	TCACGTGTAGCAGGTAGCCCT TT (SEQ ID NO:40)	ATGGCCGCATTCCACGGTGC (SEQ ID NO:41)
KIAA0688	11	GAAGCCATCTCTGACCGGATC (SEQ ID NO:42)	TCGCCGACACCTCCA (SEQ ID NO:43)	CCACACCAATGGCACGTCAGC (SEQ ID NO:44)
カテプシンB	11	GCAGGCACACGCTGCAGATA (SEQ ID NO:45)	CCTGTGGATGCATTGATTGC (SEQ ID NO:46)	TCCATTCACTCTCCGCTCTCTCAGC (SEQ ID NO:47)
プラズミノーゲンアクチベーター インヒビター-2 (PAI-2)	14			
トランスボーター-1/チヤンネル ホワイトプロテイン相関体	25	CCCTTTCAGATCATGTTCCCA (SEQ ID NO:48)	GGACGCTGGGACGTC (SEQ ID NO:49)	CCAGTACCGATGCTGCAGTAGGCCA (SEQ ID NO:50)
細胞骨格/運動性 モエシン	4	ACTGGGCGGAGACAAATACA A (SEQ ID NO:51)	AATGCGCTGCTTGGTGTG (SEQ ID NO:52)	CCCTGCGCCAGATCCGCGC (SEQ ID NO:53)
アクチン細胞タンパク質	8	CCAGCTGCTACTTTGACATCG A (SEQ ID NO:54)	CCATTGGAGCCCTCAGT (SEQ ID NO:55)	GATGCGCCGGTCAACCCCA (SEQ ID NO:56)
T-プラスチン	7	AATAAAACAGCCATGCTCCC A (SEQ ID NO:57)	CCTTAAGCCATAAGCACTTCA CC (SEQ ID NO:58)	TGCATGATTTCGAGGTCAAGCTA TTTCC (SEQ ID NO:59)
脂質キリン-2	10	AAGCAGCTTCTGATGCATTG (SEQ ID NO:60)	CGGACACAGCGCTTACAT (SEQ ID NO:61)	TCGCAGCCAAAGAACGCCACC A (SEQ ID NO:62)
中間フィラメント 中皮ケラチンK7	5	CCCAGATCTCCGACACATCTG (SEQ ID NO:63)	GCGATGATGCCGTCCAG (SEQ ID NO:64)	CCATGGACAAACAGTCCCTCCCTGG (SEQ ID NO:65)
細胞外マトリクス ラミニンB2 (ニセインB2類)	2	GCTGACAGCAGGTGTTTGA A (SEQ ID NO:66)	CGAAGTAGCTGCTTTGCACT (SEQ ID NO:67)	TGTATCCACACACAGCCGGCATCTACTG (SEQ ID NO:68)
ニドゲン-2 (ネオマトゲン)	1	AAATCTTAGAACTTTTGTG GGAAACTA (SEQ ID NO:69)	CCTTGACAGTTGGAGAGCC A (SEQ ID NO:70)	AAATAAATGGTCTTTTCCCATCAGTTCTGCCA (SEQ ID NO:71)

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INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US 00/30051

A. CLASSIFICATION OF SUBJECT MATTER		
IPC 7	C12Q1/68 C12N5/10	A61K39/00 C07K14/47 A61K48/00 G01N33/53 C07K16/18 C12N15/63
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols)		
IPC 7 C07K C12Q		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)		
MEDLINE, SEQUENCE SEARCH, EPO-Internal		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KOHFELDT E ET AL: "NIDOGEN-2: A NEW BASEMENT MEMBRANE PROTEIN WITH DIVERSE BINDING PROPERTIES" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 282, 1998, pages 99-109, XP002928990 ISSN: 0022-2836 abstract; figures 1,5; table 1 page 103, right-hand column -page 104, left-hand column, paragraph 1 page 105, right-hand column -page 107, right-hand column; figures 7-9 --- -/-	1-30, 32-37, 39-42, 44-59
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "C" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "Z" document member of the same patent family		
Date of the actual completion of the international search		Date of mailing of the international search report
20 March 2002		02. 07. 2002
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2200 LV Rijswijk Tel: (+31-70) 340-2060, Tx: 31 051 opto nl, Fax: (+31-70) 340-8015		Authorized officer van Klompenburg, W

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US 00/30051

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BIRD IAN M ET AL: "Homophilic PECAM-1(CD31) interactions prevent endothelial cell apoptosis but do not support cell spreading or migration." JOURNAL OF CELL SCIENCE, vol. 112, no. 12, June 1999 (1999-06), pages 1989-1997, XP002193379 ISSN: 0021-9533 abstract	1-30, 32-37, 39-42, 44-59
A	WO 97 30065 A (MILLENNIUM PHARM INC) 21 August 1997 (1997-08-21) page 1, line 8 - line 27 page 10, line 23 - line 29 page 12, line 33 -page 13, line 6 page 57, line 23 -page 92, line 3 claims 12-69	1-30, 32-37, 39-42, 44-59
A	WO 98 31709 A (GERL MARTIN ;HOECHST AG (DE)) 23 July 1998 (1998-07-23) page 1; claims 34-42; example 7	1-30, 32-37, 39-42, 44-59
A	WO 93 23075 A (ONCOLOGIX INC ;UNIV OHIO STATE RES FOUND (US); LIANG CHI MING (US)) 25 November 1993 (1993-11-25) page 1 -page 2, line 3 page 40, line 25 -page 42, line 19 abstract; claims 1-39; example 9	1-30, 32-37, 39-42, 44-59
P,X	WO 00 52051 A (AVENTIS PHARMA GMBH) 8 September 2000 (2000-09-08) page 1, line 4 - line 24 claims 1-97; table 2	30,33, 34,37, 39-41, 47-59
P,X	WO 00 55174 A (HUMAN GENOME SCIENCES INC ;ROSEN CRAIG A (US); RUBEN STEVEN M (US)) 21 September 2000 (2000-09-21) page 1 -page 4 page 387, line 14 -page 399, line 27 seq id no 1 & 941 claims 1-23; tables 1,4	9-30, 32-37, 39-42, 44-59

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INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US 00/30051

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 01 73025 A (BETH ISRAEL HOSPITAL ; KALLURI RAGHURAM (US)) 4 October 2001 (2001-10-04) page 2, line 10 -page 6, line 6; claims 1-36; figure 1 -----	30, 33, 34, 37, 39-41, 47-59

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/30051**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-30, 32-37, 39-42, 44-59 partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 1-29, are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Although claims 30-34, 54-59 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Present claims 30-34, 51-59 relate to a product defined by reference to a desirable characteristic or property, namely: a product that modulates the expression or activity of the nucleic acid of the invention.

The claims cover all products having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the products mentioned in the description at pages 41, lines 23-25, namely antibodies, antibody fragments, fragments or variants of PA polypeptides, peptides, antisense molecules.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims 1-30,32-37,39-42,
44- 59 partially

Invention 1 is characterized by Nidogen-2 (PA 1).
A method of assessing the efficacy of an angiogenic disorder treatment in a subject comprising identifying a difference in expression levels of PA 1. A method of diagnosing an angiogenic disorder. A method of identifying a test therapeutic agent. A method of diagnosing or determining the susceptibility to an angiogenic disorder. A method of treating an angiogenic disorder. A kit for detecting two or more nucleic acid sequences comprising PA 1. An array of probe nucleic acids, wherein said probes detect two or more nucleic acid sequences comprising PA 1. An isolated polypeptide used to treat an angiogenic disorder. An isolated nucleic acid used to treat an angiogenic disorder. A therapeutic composition comprising the above mentioned polypeptide and a carrier. A kit comprising a therapeutic composition. A method of treating an angiogenic disorder. A method for inhibiting angiogenesis. A method for stimulating angiogenesis.

Inventions 2-26: Claims 1-59 partially

The subject matter of the individual inventions 2-26 are characterized by the individual sequences of PA 2-26. Claims 31, 32, 38, 39 43, 44 are with the appropriate sequences (for instance: claim 31 with invention 5,14,15 for PA 5,14 and 15 respectively). Therefore, all of claims 1-59 belong all partially to a separate invention. The description of the subject matter is as for invention 1, but for the individual PA's.

Invention 27: claims 60-66 completely, claims 1-30,
33-37,40-42,45-59 partially

As for invention 1, but for PA 27 and additionally:
An isolated nucleic acid molecule that is at least 75% identical to a nucleic acid sequence encoding the polypeptide of SEQ ID NO: 27. A nucleic acid vector, a host cell, an isolated peptide, an antibody, a pharmaceutical composition. A method of detecting the presence of the above mentioned polypeptide or nucleic acid in a sample

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.

PCT/US 00/30051

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9730065	A	21-08-1997	AU 725192 B2 05-10-2000
			AU 2124397 A 02-09-1997
			CA 2247246 A1 21-08-1997
			EP 0904277 A1 31-03-1999
			JP 2001521365 T 06-11-2001
			WO 9730065 A1 21-08-1997
			US 6099823 A 08-08-2000
			US 6359194 B1 19-03-2002
			US 2002016303 A1 07-02-2002
			US 6048709 A 11-04-2000
			US 2002034736 A1 21-03-2002
			US 6221628 B1 24-04-2001
			US 6087477 A 11-07-2000
WO 9831709	A	23-07-1998	DE 19701607 A1 23-07-1998
			AU 5985398 A 07-08-1998
			BR 9714207 A 28-03-2000
			CN 1244873 A 16-02-2000
			CZ 9902538 A3 13-10-1999
			WO 9831709 A1 23-07-1998
			EP 0954535 A1 10-11-1999
			RU 0001808 A2 28-09-2000
			JP 2001509020 T 10-07-2001
			PL 334956 A1 27-03-2000
			TR 9901648 T2 21-10-1999
			US 2001007020 A1 05-07-2001
			ZA 9800367 A 17-07-1998
WO 9323075	A	25-11-1993	AU 4373993 A 13-12-1993
			EP 0642353 A1 15-03-1995
			WO 9323075 A1 25-11-1993
			US 5866570 A 02-02-1999
WO 0052051	A	08-09-2000	EP 1070727 A1 24-01-2001
			AU 3157700 A 21-09-2000
			BR 0008647 A 22-01-2002
			CN 1342167 T 27-03-2002
			CZ 20013063 A3 14-11-2001
			WO 0052051 A1 08-09-2000
			EP 1157040 A1 28-11-2001
			TR 200102560 T2 21-01-2002
			US 6365572 B1 02-04-2002
WO 0055174	A	21-09-2000	AU 3395900 A 04-10-2000
			AU 3617600 A 04-10-2000
			AU 3617700 A 04-10-2000
			AU 3619400 A 04-10-2000
			AU 3619500 A 04-10-2000
			AU 3869400 A 04-10-2000
			EP 1168917 A2 09-01-2002
			EP 1165588 A1 02-01-2002
			EP 1169469 A1 09-01-2002
			EP 1165589 A1 02-01-2002
			EP 1159420 A1 05-12-2001
			EP 1163358 A1 19-12-2001
			WO 0055173 A1 21-09-2000
			WO 0055350 A1 21-09-2000
			WO 0055351 A1 21-09-2000

Form PCT/ISA/210 (patent family areas) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.

PCT/US 00/30051

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0055174 A		WO 0055180 A2	21-09-2000
		WO 0055174 A1	21-09-2000
		WO 0055320 A1	21-09-2000
		US 2002039764 A1	04-04-2002
		US 2002055627 A1	09-05-2002
		US 2002052308 A1	02-05-2002
		US 2002044941 A1	18-04-2002
WO 0173025 A	04-10-2001	AU 8727401 A	08-10-2001
		WO 0173025 A2	04-10-2001

[illegible]

Activity	Hours (Number of Dots)
Reading	4
Watching TV	8
Playing Video Games	6
Homework	2
Walking the Dog	1
Eating	3
Sleeping	9
Brushing Teeth	2

[illegible]